Applicant: Aki Kitagawa et al

Serial No.: 09/834,103 Filed: April 12, 2001

Page

· 2 of 8

In the claims:

Please amend the claims as follows:

- 1. Withdrawn.
- 2. Withdrawn.
- 3. Withdrawn.
- 4. Withdrawn.
- 5. Withdrawn.
- 6. Withdrawn.
- 7. Withdrawn.
- 8. Withdrawn.
- 9. Withdrawn.
- 10. Withdrawn.
- 11. Withdrawn.
- 12. (Currently Amended) A method of producing a sustained release <u>protein</u> drug composition, the method comprising

Attorney's Docket No.: 12372-002001

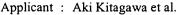
providing a precipitating solution containing a mucopolysaccharide, a carrier protein, and a <u>protein</u> drug;

lowering the pH of the precipitating solution to a <u>pH of about 3</u> level sufficient to form an insoluble product comprising the mucopolysaccharide, the carrier protein, and the <u>protein</u> drug; and

collecting from the precipitating solution the insoluble product.

13. (Original) The method of claim 12, wherein the insoluble product consists of the mucopolysaccharide, the carrier protein, the drug, and one or more pharmaceutically acceptable additives.





Serial No.: 09/834,103

Filed

: April 12, 2001

: 3 of 8 Page

(Original) The method of claim 12, wherein the ratio of the total mass of 14. mucopolysaccharide in the insoluble product to the total mass of carrier protein in the insoluble product is about 1:1 to 1:20.

Attorney's Docket No.: 12372-002001

- 15. (Original) The method of claim 12, wherein the mucopolysaccharide is chondroitin sulfate or hyaluronate.
- (Original) The method of claim 12, wherein the carrier protein is a g-globulin, 16. albumin, fibrinogen, histone, protamine, gelatin, or collagen.
 - 17. (Original) The method of claim 12, wherein the carrier protein is a g-globulin.
 - 18. (Original) The method of claim 12, wherein the carrier protein is an albumin.
 - 19. (Cancelled) The method of claim 12, wherein the drug is a protein drug.
- 20. (Original) The method of claim 12, wherein the protein drug is an erythropoietin, granulocyte colony stimulating factor, granulocyte-macrophage colony stimulating factor, thrombopoietin, interferon-a, interferon-b, interferon-g, urokinase, tissue plasminogen activator, interleukin-11, fibroblast growth factor, epidermal growth factor, growth hormone, brain-derived neurotrophic factor, nerve growth factor, leptin, neurotrophin-3, superoxide dismutase, antibody, calcitonin, insulin, or parathyroid hormone.
- 21. (Original) The method of claim 12, wherein the pH of the solution is about 7 or above before the lowering step.
- 22. (Cancelled) The method of claim 12, wherein the pH of the solution is lowered to about 2 to 4 in the lowering step.



Applicant: Aki Kitagawa et al. Attorney's Docket No.: 12372-002001

Serial No.: 09/834,103 Filed: April 12, 2001

Page : 4 of 8

23. (Original) The method of claim 12, further comprising, prior to the providing step, mixing a first solution containing the carrier protein and the drug with a second solution containing the mucopolysaccharide to produce the precipitating solution.

- 24. (Original) The method of claim 12, wherein the precipitating solution contains zinc or calcium ions.
- 25. (Original) The method of claim 12, further comprising suspending the insoluble product in a preparatory solution having a pH of about 6 to 8 to form a mixture; and

lyophilizing the mixture to obtain a solid product.

- 26. Withdrawn.
- 27. Withdrawn.
- 28. Withdrawn.
- 29. Withdrawn.
- 30. Withdrawn.
- 31. Withdrawn.
- 32. Withdrawn.
- 33. Withdrawn.
- 34. Withdrawn.
- 35. Withdrawn.
- 36. Withdrawn.
- 37. Withdrawn.
- 38. Withdrawn.
- 39. Withdrawn.
- 40. Withdrawn.
- 41. Withdrawn.
- 42. Withdrawn.
- 43. Withdrawn.



Applicant: Aki Kitagawa et al.
Serial No.: 09/834,103
Filed: April 12, 2001
Page: 5 of 8

44. Withdrawn.

45. Withdrawn.

46. Withdrawn. Attorney's Docket No.: 12372-002001